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Original article

Cholecystectomy increases the risk of dumping syndrome and postbariatric hypoglycemia after bariatric surgery

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Abstract

Background: Dumping syndrome (DS) and postbariatric hypoglycemia (PBH) are frequent complications of bariatric surgery. Bile acids (BA) have been implicated in their pathogenesis because both bariatric surgery and cholecystectomy (CCx) are known to modulate human BA metabolism.
Objectives: Our investigation aimed to compare the prevalence of self-reported complaints of DS and PBH in postbariatric patients with and without CCx.
Setting: A large peripheral hospital in the Netherlands.
Methods: All patients who underwent bariatric surgery in 2008–2011 received standardized questionnaires on DS/PBH complaints. The relative risk (RR) of CCx was calculated as the risk of perceived DS and PBH in patients with and without CCx.
Results: Of 590 participants, 146 (25%) had CCx before assessment of DS/PBH complaints. Participants were mostly female (82%) with median age of 46 years (interquartile range, 39–53). The RR for DS after CCx was higher in patients with body mass index <30 kg/m^2 at the study (RR, 1.59; 95% CI, 1.04–2.42; $P = .007$) and in primary Roux-and-Y gastric bypass surgery patients (RR, 1.63; 95% CI, 1.10–2.42; $P = .018$). Detailed analysis of the latter group associated women, age younger than 50 years, without diabetes and (most prominently) with excess weight loss $\geq$70% (RR, 2.73; 95% CI, 1.57–4.77; $P = .0004$) with greater risk of DS. The RR for PBH was higher after CCx in sleeve gastrectomy patients (RR, 4.5; 95% CI, 1.00–20.3; $P = .036$).
Conclusion: High suspicion of DS and PBH after CCx is increased after bariatric surgery in certain subgroups, suggesting involvement of altered BA metabolism in their pathophysiology. (Surg Obes Relat Dis 2020; ■:1–9.)

Keywords: Cholecystectomy; Dumping syndrome; Postbariatric hypoglycemia; Bariatric surgery; Gastric bypass; Bile acids

Morbid obesity is a rapidly increasing healthcare problem, and currently 13% of the world's population is estimated to be obese [1]. Bariatric surgery is considered to be the most effective treatment for morbid obesity in the long-term and its application has increased, with more than half a million procedures worldwide in 2016 [2,3].

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Despite the positive outcomes of bariatric surgery on weight and obesity-associated morbidities, complications such as dumping syndrome (DS) and postbariatric hypoglycemia (PBH), also known by the less preferred terminology of "early and late dumping," are common [4,5]. Both are categorized as symptoms from the same dumping disease spectrum and cannot always be discretely separated, whereby patients can develop DS, PBH, or both [6]. DS typically develops directly after the bariatric operation [7]. The classic combination of abdominal and vasomotor symptoms occurs within 1 hour after a meal. Its onset has been attributed to the entrance of undigested food into the small bowel, which in turn leads to an osmotic response followed by a decrease in plasma volume, triggering the vasomotor response [8]. We also showed the involvement of gut hormones glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) in patients with typical DS symptoms to explain the abdominal complaints in particular [9].

In contrast to DS, PBH is thought to develop months or even years after bariatric surgery [6]. It is defined by a symptomatic hypoglycemic event arising 1–3 hours after a meal, induced by disproportionately elevated insulin concentrations [10]. Both insulin sensitivity and beta cell function are important conditions found to set the stage in these patients [11]. Furthermore, GLP-1 is assumed to play a more pivotal role in the pathophysiology of PBH because the GLP-1 antagonist exendin 9-39 prevents hypoglycemia in people with severe symptoms [12].

Interestingly, bile acids (BAs) have recently been shown to play a role in the secretion of GLP-1 and other gut hormones, such as PYY, and therefore also may contribute to the pathophysiology of both syndromes [13]. BAs are known to increase GLP-1 excretion via binding to the G protein–coupled bile acid receptor (GPBAR-1), also known as TGR5, localized at enteroendocrine L-cell [14]. Numerous studies have shown that BA metabolism changes and its concentration increases in the systemic circulation after Roux-en-Y gastric bypass (RYGB), biliopancreatic diversion, and possibly vertical sleeve gastrectomy (SG) [15]. After cholecystectomy (CCx), some but not all patients have reported an altered BA metabolism because of elevated enterohepatic recycling of BA and elevated plasma BA [16]. Furthermore, bile diversion to the ileum improves glucose homeostasis by modulating GLP-1 secretion [17].

With this information, we speculated that postbariatric patients after CCx were more likely to experience symptoms related to DS or PBH. To address this, we evaluated self-reported complaints of both syndromes in relation to CCx in a large cohort of postbariatric patients.

Methods

Study population

For this retrospective cohort study, data were collected at the bariatric department in the Medical Center Leeuwarden, the Netherlands. A preexisting database was used [5], collated from the results of a questionnaire survey on self-reported early and late dumping complaints completed by all patients who underwent bariatric surgery for morbid obesity at a teaching hospital in the northern Netherlands between 2008 and 2011.

All patients were screened before their operation according to the criteria outlined by the International Federation for Surgery of Obesity and Metabolic Disorders [18]. In 2013, all patients were invited by mail to participate in a questionnaire survey. The first outcomes have already been published [5]. For the purpose of this study, patients who underwent a primary RYGB, SG, or revisional RYGB (after prior gastric banding) between 2008 and 2011 were selected. They were aged between 18–75 years. Those who had undergone extra revisional surgery or who had incomplete data were excluded. An additional data set, collected in 2018 through the EPIC electronic health record, contained details on the patients' prior CCx. Written informed consent was obtained from all participants. The study protocol was approved by the Regional Ethical Review Board of the Medical Centre Leeuwarden (registered at ISRCTN17666669).

Surgical technique – bariatric procedures

In all patients a standardized operation technique was used, and all 3 surgeons complied with this standard. The techniques for primary and revisional gastric bypass have previously been described [5]. In short, we created a pouch of approximately 30–60 cc in primary gastric bypass. After revisional bypass, this pouch was extended to 60–80 cc because we started the creation of the pouch beneath the scar tissue of the former banding. The band placing was mostly done via the pars flaccida technique, in which the anterior and posterior nerves of Latarjet were not preserved. In both procedures we used the omentum-sparing procedure for creating the pouch, in which the lesser sac was entered via perigastric dissection with care taken to preserve the anterior and posterior nerves of Latarjet.

The other difference with the primary RYGB technique is that we covered all our anastomosis at the end of the revisional procedure with tissue col (Baxter, Utrecht, the Netherlands). Karmali et al. earlier described the SG technique [19]. We started transection at 6 cm before the pylorus and used a 34-F gastric tube for calibration of the sleeve. The sleeve was made "floppy" around this tube. In all procedures, the integrity of the anastomoses or staple line was monitored by methylene and air leak testing after introduction of a gastric tube by the anesthesiologist. In case of leakage, additional sutures were placed.

Cholecystectomy

The patients in our cohort underwent their CCx in many different regional hospitals. Assessment of this

procedure was based on critical review of the medical charts. In general, the guideline for treatment of gallbladder stones in the Netherlands supports the use of the critical view of safety, in which 3 requirements must be met before the cystic duct and artery can be ligated and cut [20]. Most of the patients had been operated on laparoscopically because it is the preferred surgery type. All patients were operated on under high suspicion of symptomatic cholecystolithiasis.

Questionnaires

The dumping severity score developed by Arts et al. was used for assessment of the severity of DS and PBH [21]. This questionnaire uses a 4-point Likert scale. Patients were asked to grade the intensity (0 = absent; 1 = mild; 2 = moderate, and 3 = severe, i.e., interfering with daily activities) of 8 complaints related to DS within 1 hour of food ingestion and of 6 hypoglycemia-related complaints >1 hour after food ingestion. For DS, the complaints were abdominal pain, diarrhea, bloating (3 abdominal symptoms), nausea, sweating, flushing, dizziness, and palpitations (5 autonomic symptoms). For PBH, they were sweating, palpitations, hunger, tremor (4 autonomic symptoms), drowsiness/unconsciousness, and irritability (2 neuroglycopenic symptoms). Based on the results of this questionnaire, patients were classified in 2 groups: high and low suspicion of either DS or PBH.

We defined high suspicion of DS as someone with ≥3 moderate or severe symptoms (including ≥1 autonomic symptom) on the early dumping severity score. A high suspicion of PBH was defined with the presence of ≥3 moderate or severe symptoms (including ≥1 neuroglycopenic symptom) on the late dumping severity score. In a separate analysis, the total scores were calculated as the sum of the intensity grades of each individual component of DS and PBH.

Additional questions were asked regarding weight development and co-morbidities, including on the use of medication. These data were checked against the data collected at the last outpatient visit and in the electronic patient records.

The number of patients for primary RYGB, SG, and revisional RYGB was 352, 88, and 150, respectively. Background prevalences of DS and PBH for primary RYGB, SG, and revisional RYGB were 19.4%, 9.1%, 23.5% and 11.4%, −6.7%, −20.3%, respectively [5].

Disease terminology

In line with Rogowitz et al., we preferred to adopt the terminology "dumping syndrome" instead of "early dumping," and "postbariatric hypoglycemia" instead of "late dumping" [4]. For the dumping severity score questionnaire, the original denotation was used, that is, "early and late dumping," together with the preferred terminology.

Statistics

Data are presented as mean (SD), median (interquartile range), frequencies, or percentages where appropriate. Differences were assessed with Mann-Whitney *U* tests (for continuous variables) or χ^2 tests (for categoric variables). A P value < .05 was used for determining statistical significance. Relative risks (RRs) were calculated (mean with 95% CIs) by comparing the prevalence of high suspicion for DS and BPH between patients with and without CCx (the comparator). All statistical analysis was performed using SPSS version 24 (IBM, Armonk, NY). For graphic presentations, GraphPad Prism version 5 (GraphPad Software Inc., La Jolla, CA) was used.

Results

Patient characteristics (Table 1, Fig. 1)

The questionnaire was completed and returned by 590 of the 1046 patients (57%) approached. The patient characteristics are presented in Table 1. A total of 146 (25%) underwent a CCx. Participants were mostly female (82%), with a median age of 46 years (interquartile range, 39–53 years) at the time of the survey. Most CCx (70%) were carried out before bariatric surgery. Fig. 1 shows the cumulative number of CCx versus time between CCx and the final bariatric procedure. There is a 2- to 8-fold increase in the yearly incidence of CCx in the 0–2 years after the bariatric procedure compared with before the procedure. In the group with CCx, significantly more patients were female (91% versus 79%, P = .001). No differences between the bariatric patient groups with and without CCx were found in body mass index (BMI) at the time of bariatric surgery and in the weight loss thereafter (Table 1).

Perceived complaints of DS and PBH in all patients (Tables 2 and 3, Fig. 2)

The bariatric patients after CCx showed a trend toward a higher RR for perceived DS complaints than bariatric patients without a CCx (RR, 1.32; 95% CI, .96–1.82; P = .088). Additionally, in a subgroup analysis of these patients, the RR was significantly higher for patients with a primary RYGB (RR, .018; 95% CI, 1.10–2.42; P = .018), BMI >30 kg/m^2 (RR, 1.59; 95% CI, 1.04–2.42; P = .007), BMI loss ≥14 kg/m^2 (RR, 1.60; 95% CI, 1.04–2.50; P = .038), and excess weight loss (EWL) ≥70% (RR, 1.88; 95% CI, 1.21–2.932; P = .0067). This is also illustrated by a right shift in the cumulative distribution of the total early dumping score (Fig. 2, right panel) for the subgroup of BMI <30 kg/m^2. An effect of the CCx on complaints of DS was not seen in the subgroups by age (<50 or ≥50), sex, or prior diabetes.

For all patients, there was no difference found in the risk of perceiving complaints of PBH between the groups with or without CCx. The only exception was in the subgroup BMI

Table 1
Patient characteristics

	Total	Cholecystectomy yes	Cholecystectomy no	*P* value
All patients	590 (100)	146 (25)	444 (75)	
Female, n (%)	483 (82)	133 (91)	350 (79)	.001
Age at time of study, yr	46 (39 to 53)	45 (39 to 55)	46 (38 to 52)	.413
Weight and weight loss				
Weight at bariatric surgery, kg	129 (116 to 143)	127 (117 to 142)	129 (116 to 144)	.820
BMI at bariatric surgery, kg/m^2	43 (40 to 48)	44 (41 to 48)	43 (40 to 48)	.473
BMI at study, kg/m^2	30 (26 to 34)	30 (26 to 34)	30 (26 to 34)	.779
BMI loss, kg/m^2	14 (10 to18)	14 (11 to 18)	14 (10 to 18)	.959
Timing of surgery				
Time between survey and bariatric surgery, mo (m)(m)	26 (19 to 35)	26 (19 to 35)	26 (19 to 34)	.943
Time between survey and CCx, mo		61(23 to 109)		
Time between CCx and bariatric surgery, mo		−36 (−90 to 8)		
CCx before bariatric surgery, n (%)		96 (70)		

CCx = cholecystectomy; BMI = body mass index.
Data are median (interquartile range) or number (%).

loss >14 kg/m^2 (RR, 1.80; 95% CI, 1.01–3.20; P = .046) and after SG (RR, 4.5; 95% CI, 1.00–20.3; P = .036).

Perceived complaints of DS and PBH in primary RYGB patients (Tables 4 and 5)

The risk of perceiving complaints of DS was increased after CCx in all primary RYGB patients (RR, 1.63; 95% CI, 1.10–2.42; P = .018) and in the following subgroups (Table 4): women (RR, 1.59; 95% CI, 1.06–2.40; P = .026), age younger than 50 years (RR, 1.68; 95% CI, 1.03–2.73; P = .042), without prior diabetes (RR, 1.85; 95% CI, 1.17–2.94; P = .010), with a BMI <30 at the study (RR, 2.23; 95% CI, 1.37–3.62; P = .002), with higher BMI loss (RR, 1.79; 95% CI, 1.04–3.08; P = .039), and higher EWL (RR, 2.73; 95% CI, 1.57–4.77; P = .0004).

No effects of CCx were observed related to the risk of perceiving complaints of PBH in all patients or in their subgroups after primary RYGB.

Discussion

This is the first clinical study describing the effects of various bariatric procedures in combination with CCx on

Cumulative distribution (percentage of patients) of time between cholecystectomy and bariatric surgery.

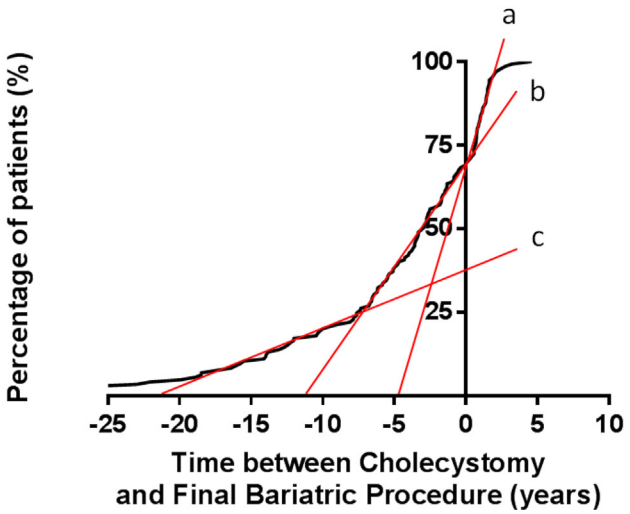

Fig. 1. Cumulative distribution (percentage of patients) of time between cholecystectomy and bariatric surgery. a = 20 procedures/year, b = 10/year, c = 2.5/year. Note the increase in yearly incidence rate directly after bariatric surgery.

Table 2
Analysis of all patients with or without cholecystectomy on risk of complaints of dumping syndrome

	Total	Cholecystectomy yes		Cholecystectomy no		Relative risk (95% CI)	*P* value
		Dumping syndrome +	Dumping syndrome −	Dumping syndrome +	Dumping syndrome −		
All patients	588	40	105	92	351	1.32 (.96-1.82)	.088*
Sex							
Female	481	38	94	78	271	1.29 (.92-1.80)	.141
Male	107	2	11	14	80	1.03 (.26-4.04)	.963
Age							
≥50 yr	214	14	43	28	129	.86 (.51-1.46)	.273
<50 yr	373	26	62	64	221	1.32 (.89-1.94)	.174
Prior diabetes							
Yes	150	9	27	22	92	1.30 (.66-2.55)	.461
No	437	31	78	70	258	1.33 (.93-1.92)	.128
Procedure							
pRYGB	351	29	66	48	208	1.63 (1.10-2.42)	.018*
SG	87	1	15	10	61	.44 (.06-3.22)	.394
rRYGB	150	10	24	34	82	1.00 (.55-1.81)	.991
BMI at study							
≥30 kg/m^2	281	14	56	49	162	.86 (.51-1.46)	.575
<30 kg/m^2	303	25	49	43	186	1.59 (1.04-2.42)	.007*
BMI loss							
≥14 kg/m^2	313	22	51	45	195	1.60 (1.04-2.50)	.038*
<14 kg/m^2	275	18	54	47	156	1.08 (.67-1.73)	.751
EWL							
≥70%	280	25	52	35	168	1.88 (1.21-2.93)	.006*
<70%	278	13	49	51	165	.89 (.52-1.52)	.663

pRYGB = primary Roux-en-Y gastric bypass; SG = sleeve gastrectomy; rRYGB = revisional Roux-en-Y gastric bypass (with prior gastric banding); BMI = body mass index; EWL = excess weight loss from primary procedure to study.
* $P < .05$.

perceived complaints of DS and PBH. We found that CCx in combination with various procedures and patient characteristics (such as type of surgery, women, younger age, lower BMI, and more weight loss) presents an increased risk for perceived complaints of DS. Similarly, patients with both an SG and a CCx are at higher risk of perceiving complaints of PBH. Because both bariatric surgery and CCx are associated with marked alterations in BA metabolism and because BAs have been implicated in the control of GLP-1-mediated insulin release, our results imply a role for BA in the etiologies of DS and PBH.

The gallbladder has an important function in BA homeostasis. Removal of the gallbladder has been shown to increase fasting and postprandial synthesis of plasma BA and levels of C4, a BA synthesis biomarker [16]. According to a systematic review, RYGB surgery increases the fasting concentration of total BA, which is suggested to be beneficial to metabolic health [22]. Furthermore, SG also leads to increased BA levels [23]. Several lines of evidence suggest a role for BA in glucose metabolism. BA stimulate the release of fibroblast growth factor 19, which is thought to be involved in glycogen synthesis and glucose disposal [24]. Correspondingly, fibroblast growth factor 19 levels after a mixed meal were found to be more than twice as high in patients with PBH than in patients without hypoglycemia [25]. Through activation of GPBAR-1, expressed among others on the enteroendocrine L-cells, BA also stimulates the release of GLP-1 and PYY [14,26]. After RYGB, accelerated and increased elevations of postprandial plasma concentrations of GLP-1 and PYY have been reported [27]. In agreement, GLP-1 mediates the postprandial (hyper) secretion of insulin, which in turn contributes to causing PBH [28]. Therefore, both RYGB and CCx could be acting synergistically through altered BA metabolism in the stimulation of postprandial glucose metabolism leading to PBH. Furthermore, DS during a mixed meal tolerance test is considered to be related to GLP-1 and PYY [9]. Therefore, the synergistic effect of RYGB and CCx could also play a role in the development of DS complaints.

Indeed, we found an increased RR of both DS and for PBH in several subgroups of bariatric patients with a CCx compared with those without CCx. These results warrant further research in this area, specifically regarding interventions such as cholestyramine, a BA sequestrant for the treatment of DS and PBH. Also of interest is that several risk factors previously found to be of importance in the multifactorial pathogenesis of PBH were associated with increased risk of DS, including younger age, sex, BMI, EWL and no history of diabetes [11]. As outlined, these findings fit in a common etiology in which similar (hormonal) pathways

Table 3
Analysis of all patients with or without cholecystectomy on risk of complaints of PBH

	Total	Cholecystectomy yes		Cholecystectomy no		Relative risk (95% CI)	*P* value
		PBH +	PBH −	PBH +	PBH −		
All patients	590	24	122	53	391	1.38 (.88-2.15)	.161
Sex							
Female	483	22	111	47	303	1.23 (.77-1.96)	.383
Male	107	2	11	6	88	2.41 (.54-10.70)	.247
Age							
≥50 yr	215	9	48	13	145	1.92 (.87-4.25)	.106
< 50 yr	374	15	74	40	245	1.20 (.70-2.07)	.512
Prior diabetes							
Yes	150	6	13	30	101	1.38 (.66-2.87)	.408
No	439	18	92	40	289	1.35 (.81-2.25)	.259
Procedure							
pRYGB	352	14	82	26	230	1.43 (.78-2.63)	.244
SG	88	3	13	3	69	4.50 (1.00-20.30)	.036*
rRYGB	150	7	27	24	92	1.00 (.47-2.11)	.990
BMI at study							
≥30 kg/m^2	282	12	58	29	183	1.25 (.68-2.32)	.476
<30 kg/m^2	304	12	63	24	205	1.52 (.80-2.90)	.199
BMI loss							
≥14 kg/m^2	314	15	59	27	213	1.80 (1.01-3.20)	.046*
<14 kg/m^2	276	9	63	26	278	1.46 (.72-2.98)	.957
EWL							
≥70%	282	14	64	25	179	1.46 (.80-2.67)	.215
<70%	278	9	53	25	191	1.25 (.62-2.55)	.533

PBH = postbariatric hypoglycemia; pRYGB = primary Roux-en-Y gastric bypass; SG = sleeve gastrectomy; rRYGB = revisional Roux-en-Y gastric bypass (with prior gastric banding); BMI = body mass index; EWL = excess weight loss from primary procedure to study.
* $P < .05$.

are involved, for example because of estrogens causing (excess) biliary cholesterol secretion.

Certain discrepancies need to be discussed. Contrary to the primary RYGB group, we did not find an effect of CCx after revisional RYGB. This discrepancy might be explained by the possibility of compromised BA secretion as a consequence of vagal nerve damage due to prior laparoscopic banding [29]. In this case, diminished BA flow could have obscured the effect of the CCx and thereby DS complaints. Furthermore, we found an abundance of

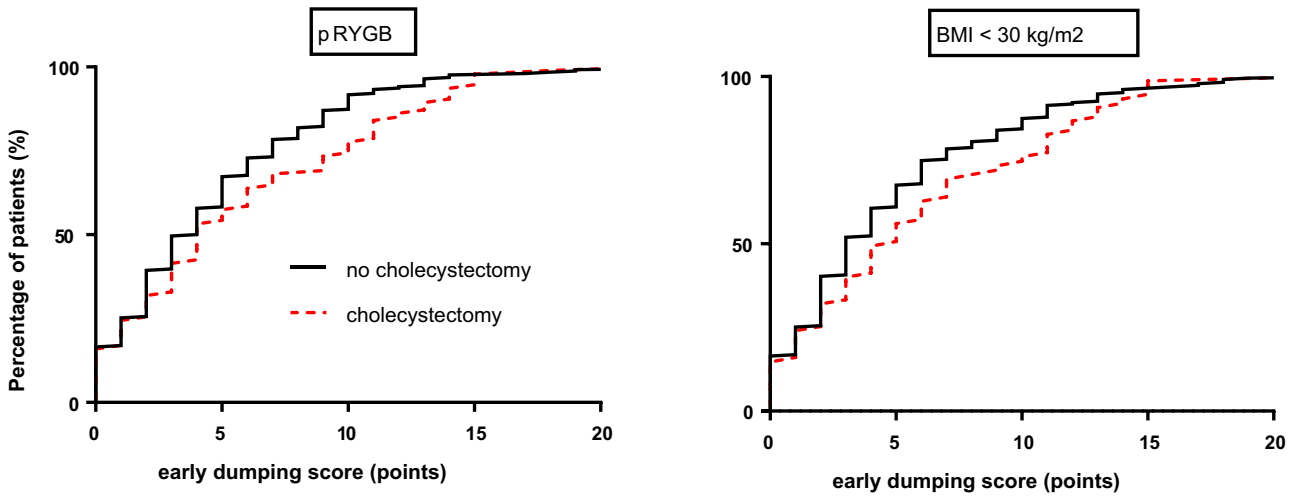

Fig. 2. Cumulative distribution of early dumping score in patients with or without cholecystectomy for primary RYGB and BMI < 30 kg/m^2 at study. pRYGB: primary Roux-en-Y gastric bypass; BMI: body mass index.

Table 4
Analysis of pRYGB patients with or without cholecystectomy on risk of complaints of dumping syndrome

	Total	Cholecystectomy yes		Cholecystectomy no		Relative risk (95% CI)	*P* value
		Dumping syndrome +	Dumping syndrome −	Dumping syndrome +	Dumping syndrome −		
All patients	351	29	66	48	208	1.63 (1.10-2.42)	.018*
Sex							
Female	282	29	59	40	154	1.59 (1.06-2.40)	.026*
Male	69	0	7	8	54	.46 (.03-7.29)	.312
Age							
≥50 yr	139	11	31	16	81	1.59 (.81-3.12)	.185
<50 yr	211	18	35	32	126	1.68 ((1.03-2.73)	.042*
Prior diabetes							
Yes	104	7	23	15	59	1.15 (.52-2.54)	.729
No	246	22	43	33	148	1.85 (1.17-2.94)	.010*
BMI at study							
≥30 kg/m^2	152	8	36	22	86	.89 (.43-1.85)	.758
< 30 kg/m^2	195	20	30	26	119	2.23 (1.37-3.62)	.002*
BMI loss							
≥14 kg/m^2	201	16	37	25	123	1.79 (1.04-3.08)	.039*
<14 kg/m^2	150	13	29	23	85	1.45 (.82-2.59)	.214
EWL							
≥70%	168	18	27	18	105	2.73 (1.57-4.77)	.0004*
<70%	164	9	35	25	95	.98 (.50-1.97)	.958

pRYGB = primary Roux-en-Y gastric bypass; BMI = body mass index; EWL = excess weight loss from primary procedure to study.
* $P < .05$.

risk factors after CCx for DS but only relatively few for PBH. In fact, the absence of typical demographic risk factors previously found for PBH is eye-catching. This is likely to be because the Arts questionnaire is not sensitive enough for cases of hypoglycemia without symptoms (i.e., hypoglycemia unawareness). In these cases, the relationship between CCx (and therefore BA) and PBH may be missed. Mild cases of recurrent hypoglycemia, without

Table 5
Analysis of pRYGB patients with or without cholecystectomy on risk of complaints of PBH

	Total	Cholecystectomy yes		Cholecystectomy no		Relative risk (95% CI)	*P* value
		PBH +	PBH −	PBH +	PBH −		
All patients	352	14	82	26	230	1.43 (.78-2.63)	.244
Sex							
Female	283	13	76	22	172	1.29 (.68-2.44)	.438
Male	69	1	6	4	58	2.21 (.29-17.2)	.449
Age							
≥50 yr	139	6	36	8	89	1.73 (.64-4.68)	.277
< 50 yr	212	8	46	18	140	1.30 (.60-2.82)	.508
Prior diabetes							
Yes	104	4	26	7	67	1.41 (.45-4.46)	.561
No	247	10	56	19	162	1.44 (.71-2.94)	.315
BMI at study							
≥30 kg/m^2	152	7	37	11	97	1.56 (.65-3.77)	.322
<30 kg/m^2	196	7	44	15	130	1.33 (.57-3.07)	.511
BMI loss							
≥14 kg/m^2	202	9	45	13	135	1.90 (.86-4.18)	.111
<14 kg/m^2	150	5	37	13	95	.99 (.38-2.60)	.982
EWL							
≥70%	169	7	39	10	113	1.87 (.76-4.62)	.173
<70%	164	6	38	13	107	1.26 (.51-3.11)	.619

PBH = postbariatric hypoglycemia; pRYGB = primary Roux-en-Y gastric bypass; BMI = body mass index; EWL = excess weight loss from primary procedure to study.

the development of hypoglycemia unawareness, may then yield significant results. We speculate that this is the reason there was a relationship with SG but not with RYGB and PBH.

Some limitations to this study should also be mentioned here. First, the participation rate was slightly less than 60%, raising the possibility of an inclusion bias. Moreover, it might be possible that some of our participants already had DS and PBH symptoms before bariatric surgery. Inherent to our cross-sectional study design we have no preoperative data on this. However, the percentage of patients participating was equal in all surgical procedure groups, and we calculated risk ratios comparing risks after bariatric surgery [5]. A second limitation relates to the fact that no validated questionnaire for early and late dumping is available [30]. The only questionnaire that is available and that differentiates between the onset of complaints after eating and these kind of symptoms is the dumping severity score, which provides a quantitative assessment of symptom severity.

The arbitrary cutoff values for DS and PBH are also debatable. However, as shown in Fig. 2, it is not only that higher prevalence above a certain cutoff level was found, but there was also a complete right shift in the cumulative scores. By calculating RRs for those with CCx compared with those without CCx, the need for validation of the questionnaire is reduced. Lastly, although this is a large study, certain subgroups were possibly too small, so their significance may also be missed.

Conclusion

In conclusion, our results suggest that bariatric patients with a prior CCx have an increased risk of complaints of DS and PBH, thereby indicating a role for altered kinetics of the circulating BA pool in the pathogenesis of these syndromes.

Disclosures

The authors have no commercial associations that might be a conflict of interest in relation to this article.

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